

Rec'd PCT/PTO 21 MAR 2002

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|---|--|---|--|--|--|
| FORM PTO-1390 (Modified) (REV 11-2000) | | U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE | | ATTORNEY'S DOCKET NUMBER 220316US0PCT | |
| TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371 | | | | U.S. APPLICATION NO. (IF KNOWN, SEE 37 CFR 10/088090 | |
| | | | | | |
| INTERNATIONAL APPLICATION NO. PCT/IB00/01382 | | INTERNATIONAL FILING DATE 28 September 2000 | | PRIORITY DATE CLAIMED 28 September 1999 | |
| TITLE OF INVENTION PHARMACEUTICALLY ACTIVE SULFONYL AMINO ACID DERIVATIVES | | | | | |
| APPLICANT(S) FOR DO/EO/US Stephen ARKINSTALL et al. | | | | | |
| Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information: | | | | | |
| <ol style="list-style-type: none"> 1. <input checked="" type="checkbox"/> This is a FIRST submission of items concerning a filing under 35 U.S.C. 371. 2. <input type="checkbox"/> This is a SECOND or SUBSEQUENT submission of items concerning a filing under 35 U.S.C. 371. 3. <input checked="" type="checkbox"/> This is an express request to begin national examination procedures (35 U.S.C. 371(f)). The submission must include items (5), (6), (9) and (24) indicated below. 4. <input checked="" type="checkbox"/> The US has been elected by the expiration of 19 months from the priority date (Article 31). 5. <input checked="" type="checkbox"/> A copy of the International Application as filed (35 U.S.C. 371 (c) (2)) <ol style="list-style-type: none"> a. <input type="checkbox"/> is attached hereto (required only if not communicated by the International Bureau). b. <input checked="" type="checkbox"/> has been communicated by the International Bureau. c. <input type="checkbox"/> is not required, as the application was filed in the United States Receiving Office (RO/US). 6. <input type="checkbox"/> An English language translation of the International Application as filed (35 U.S.C. 371(c)(2)). <ol style="list-style-type: none"> a. <input type="checkbox"/> is attached hereto. b. <input type="checkbox"/> has been previously submitted under 35 U.S.C. 154(d)(4). 7. <input checked="" type="checkbox"/> Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371 (c)(3)) <ol style="list-style-type: none"> a. <input type="checkbox"/> are attached hereto (required only if not communicated by the International Bureau). b. <input type="checkbox"/> have been communicated by the International Bureau. c. <input type="checkbox"/> have not been made; however, the time limit for making such amendments has NOT expired. d. <input checked="" type="checkbox"/> have not been made and will not be made. 8. <input type="checkbox"/> An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)). 9. <input type="checkbox"/> An oath or declaration of the inventor(s) (35 U.S.C. 371 (c)(4)). 10. <input type="checkbox"/> An English language translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371 (c)(5)). 11. <input checked="" type="checkbox"/> A copy of the International Preliminary Examination Report (PCT/IPEA/409). 12. <input checked="" type="checkbox"/> A copy of the International Search Report (PCT/ISA/210). <p>Items 13 to 20 below concern document(s) or information included:</p> <ol style="list-style-type: none"> 13. <input checked="" type="checkbox"/> An Information Disclosure Statement under 37 CFR 1.97 and 1.98. 14. <input type="checkbox"/> An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included. 15. <input checked="" type="checkbox"/> A FIRST preliminary amendment. 16. <input type="checkbox"/> A SECOND or SUBSEQUENT preliminary amendment. 17. <input type="checkbox"/> A substitute specification. 18. <input type="checkbox"/> A change of power of attorney and/or address letter. 19. <input type="checkbox"/> A computer-readable form of the sequence listing in accordance with PCT Rule 13ter.2 and 35 U.S.C. 1.821 - 1.825. 20. <input type="checkbox"/> A second copy of the published international application under 35 U.S.C. 154(d)(4). 21. <input type="checkbox"/> A second copy of the English language translation of the international application under 35 U.S.C. 154(d)(4). 22. <input type="checkbox"/> Certificate of Mailing by Express Mail 23. <input checked="" type="checkbox"/> Other items or information: Notice of Priority/ Form PTO-1449 References Cited (5) | | | | | |

| | | | | | | | |
|---|--|--|--|---------------------------------------|--|--|--|
| U.S. APPLICATION NO. (IF KNOWN, SEE 37 CFR 10/088090) | | INTERNATIONAL APPLICATION NO. PCT/IB00/01382 | | ATTORNEY'S DOCKET NUMBER 220316US0PCT | | | |
| 24. The following fees are submitted: BASIC NATIONAL FEE (37 CFR 1.492 (a) (1) - (5)) : <div><input type="checkbox"/> Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO and International Search Report not prepared by the EPO or JPO \$1040.00 <input checked="" type="checkbox"/> International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO \$890.00 <input type="checkbox"/> International preliminary examination fee (37 CFR 1.482) not paid to USPTO but international search fee (37 CFR 1.445(a)(2)) paid to USPTO \$740.00 <input type="checkbox"/> International preliminary examination fee (37 CFR 1.482) paid to USPTO but all claims did not satisfy provisions of PCT Article 33(1)-(4) \$710.00 <input type="checkbox"/> International preliminary examination fee (37 CFR 1.482) paid to USPTO and all claims satisfied provisions of PCT Article 33(1)-(4) \$100.00</div> <div>ENTER APPROPRIATE BASIC FEE AMOUNT = \$890.00</div> | | | | CALCULATIONS PTO USE ONLY | | | |
| Surcharge of \$130.00 for furnishing the oath or declaration later than months from the earliest claimed priority date (37 CFR 1.492 (e)). <input type="checkbox"/> 20 <input checked="" type="checkbox"/> 30 | | | | \$130.00 | | | |
| CLAIMS | | NUMBER FILED | | NUMBER EXTRA | | | |
| Total claims | | 28 - 20 = | | 8 | | | |
| Independent claims | | 3 - 3 = | | 0 | | | |
| Multiple Dependent Claims (check if applicable). | | <input type="checkbox"/> | | | | | |
| TOTAL OF ABOVE CALCULATIONS = | | | | \$1,164.00 | | | |
| <input type="checkbox"/> Applicant claims small entity status. See 37 CFR 1.27). The fees indicated above are reduced by 1/2. | | | | \$0.00 | | | |
| SUBTOTAL = | | | | \$1,164.00 | | | |
| Processing fee of \$130.00 for furnishing the English translation later than months from the earliest claimed priority date (37 CFR 1.492 (f)). <input type="checkbox"/> 20 <input type="checkbox"/> 30 + | | | | \$0.00 | | | |
| TOTAL NATIONAL FEE = | | | | \$1,164.00 | | | |
| Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31) (check if applicable). <input type="checkbox"/> | | | | \$0.00 | | | |
| TOTAL FEES ENCLOSED = | | | | \$1,164.00 | | | |
| | | | | Amount to be refunded \$ | | | |
| | | | | charged \$ | | | |
| a. <input checked="" type="checkbox"/> A check in the amount of \$1,164.00 to cover the above fees is enclosed. b. <input type="checkbox"/> Please charge my Deposit Account No. _____ in the amount of _____ to cover the above fees. A duplicate copy of this sheet is enclosed. c. <input checked="" type="checkbox"/> The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 15-0030 A duplicate copy of this sheet is enclosed. d. <input type="checkbox"/> Fees are to be charged to a credit card. WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038. | | | | | | | |
| NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status. | | | | | | | |
| SEND ALL CORRESPONDENCE TO: <div>Surinder Sachar Registration No. 34,423 <div><div><div></div></div><div>22850</div></div></div> | | | | | | SIGNATURE Norman F. Oblon NAME 24,618 REGISTRATION NUMBER March 21 2012 DATE | |

Docket No. 220316US0PCT

IN RE APPLICATION OF: Stephen ARKINSTALL, et al.

SERIAL NO: New U.S. PCT Application

FILED: HEREWITH

FOR: PHARMACEUTICALLY ACTIVE SULFONYL AMINO ACID DERIVATIVES

ASSISTANT COMMISSIONER FOR PATENTS
WASHINGTON, D.C. 20231

SIR:

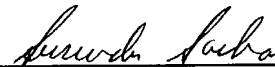
Transmitted herewith is an amendment in the above-identified application.

- ☒ No additional fee is required
- ☐ Small entity status of this application under 37 C.F.R. §1.9 and §1.27 is claimed.
- ☒ Additional documents filed herewith: PCT Transmittal Letter/Check for \$1,164.00/Notice of Priority
Information Disclosure Statement/Form PTO-1449/References Cited (5)
International Search Report/International Preliminary Examination Report

The Fee has been calculated as shown below:

The FCC has been calculated as follows:

| CLAIMS | CLAIMS REMAINING | | HIGHEST NUMBER PREVIOUSLY PAID | NO. EXTRA CLAIMS | RATE | CALCULATIONS | |
|-------------|---------------------|--|---|------------------------|-----------|--------------|--------|
| TOTAL | 28 | MINUS | 28 | 0 | × \$18 = | \$0.00 | |
| INDEPENDENT | 3 | MINUS | 3 | 0 | × \$84 = | \$0.00 | |
| | | <input type="checkbox"/> MULTIPLE DEPENDENT CLAIMS | | | + \$280 = | \$0.00 | |
| | | TOTAL OF ABOVE CALCULATIONS | | | | | \$0.00 |
| | | <input type="checkbox"/> Reduction by 50% for filing by Small Entity | | | | | \$0.00 |
| | | <input type="checkbox"/> Recordation of Assignment | | | + \$40 = | \$0.00 | |
| | | TOTAL | | | | | \$0.00 |

☐ A check in the amount of \$0.00 is attached.☒ Please charge any additional Fees for the papers being filed herewith and for which no check is enclosed herewith, or credit any overpayment to deposit Account No. 15-0030. A duplicate copy of this sheet is enclosed.☒ If these papers are not considered timely filed by the Patent and Trademark Office, then a petition is hereby made under 37 C.F.R. §1.136, and any additional fees required under 37 C.F.R. §1.136 for any necessary extension of time may be charged to Deposit Account No. 15-0030. A duplicate copy of this sheet is enclosed.OBLON, SPIVAK, McCLELLAND,
MAIER & NEUSTADT, P.C.Norman F. Oblon
Registration No. 24,618Surinder Sachar
Registration No. 34,423

22850

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(OSMMN 10/01)

220316US-0PCT

IN THE UNITED STATES PATENT & TRADEMARK OFFICE

IN RE APPLICATION OF :
 STEPHEN ARKINSTALL ET AL : ATTN: APPLICATION DIVISION
 SERIAL NO: NEW U.S. PCT APPLN :
 (Based on PCT/IB00/01382)
 FILED: HEREWITH :
 FOR: PHARMACEUTICALLY ACTIVE :
 SULFONYL AMINO ACID
 DERIVATIVES

PRELIMINARY AMENDMENT

ASSISTANT COMMISSIONER FOR PATENTS
 WASHINGTON, D.C. 20231

SIR:

Prior to examination on the merits, please amend the above-identified application as follows.

IN THE CLAIMS

Please amend the claims as shown on the marked-up copy following this amendment to read as follows.

3. (Amended) A sulfonyl amino acid derivatives according to claim 1, wherein n is 1.
4. (Amended) A sulfonyl amino acid derivative according to claim 1, wherein Ar¹ and Ar² are independently selected from the group comprising or consisting of phenyl, thienyl, furyl, pyridyl, said residues being optionally substituted by at least one substituted or unsubstituted C₁-C₆-alkyl, like trihalomethyl, substituted or unsubstituted C₁-C₆-alkoxy,

substituted or unsubstituted C₂-C₆-alkenyl, substituted or unsubstituted C₂-C₆-alkynyl, amino, acylamino, aminocarbonyl, substituted or unsubstituted C₁-C₆-alkoxycarbonyl, aryl, carboxyl, cyano, halogen, hydroxy, nitro, acyloxy, acylamino, sulfoxy, sulfonyl, substituted or unsubstituted C₁-C₆- thioalkoxy.

5. (Amended) A sulfonyl amino acid derivative according to claim 1, wherein at least one of R³ and/or R⁴ is selected from the group consisting of the following natural amino acid residues : alanyl, arginyl, asparaginy, aspartyl, cysteiny, glutaminy, glutamyl, glycyl, histidyl, isoleucyl, leucyl, lysyl, methionyl, phenylalanyl, prolyl, seryl, threonyl, tryptophanyl, tyrosyl, valyl.

6. (Amended) A sulfonyl amino acid derivative according to claim 1, wherein Ar¹ is an unsubstituted or substituted phenyl, preferably 4-chlorophenyl, X is O, R¹, R², R³ and R⁴ are hydrogen, n is 1, Ar² is thienyl, R⁵ is H or C₁-C₆-alkyl;

R⁶ is selected from the group comprising or consisting of H, a substituted or unsubstituted C₁-C₆-aliphatic alkyl - e.g. a C₁-C₆-alkylamino aryl, a C₁-C₆-alkylamino heteroaryl, a substituted or unsubstituted cyclic C₄-C₈-alkyl containing optionally 1-3 heteroatoms and being optionally fused with an unsubstituted or substituted aryl or heteroaryl; or R⁶ is an unsubstituted or substituted aryl or heteroaryl;

said aryl or heteroaryl groups are optionally substituted by substituted or unsubstituted C₁-C₆-alkyl, like trihalomethyl, substituted or unsubstituted C₁-C₆-alkoxy, substituted or unsubstituted C₂-C₆-alkenyl, substituted or unsubstituted C₂-C₆-alkynyl, amino, acylamino, aminocarbonyl, substituted or unsubstituted C₁-C₆-alkoxycarbonyl, aryl, carboxyl, cyano, halogen, hydroxy, nitro, sulfoxy, C₁-C₆- thio alkoxy; or

R⁵ and R⁶ taken together could form an unsubstituted or substituted 4-8-membered saturated cyclic alkyl or heteroalkyl group, e.g. an unsubstituted or substituted piperidino group.

7. (Amended) A sulfonyl amino acid derivative according to claim 1, wherein

R⁵ is H; and R⁶ is a C₁-C₆-alkyl which is substituted by an aryl, an heteroaryl group or an aminoaryl, aminoheteroaryl, aryloxy, heteroaryloxy, whereby said aryl and heteroaryl groups are optionally substituted by substituted or unsubstituted C₁-C₆-alkyl, like trihalomethyl, substituted or unsubstituted C₁-C₆-alkoxy, substituted or unsubstituted C₂-C₆-alkenyl, substituted or unsubstituted C₂-C₆-alkynyl, amino, acylamino, aminocarbonyl, substituted or unsubstituted C₁-C₆-alkoxycarbonyl, substituted or unsubstituted aryl, carboxyl, cyano, halogen, hydroxy, nitro, sulfoxy, C₁-C₆-thioalkoxy.

4-chloro-N-({5-[(2-({3-chloro-5-(trifluoromethyl)pyridin-2-yl}amino)ethyl)-amino]-2-oxoethyl}amino)sulfonyl]thien-2-yl}methyl)benzamide

4-chloro-N-({5-[(2-oxo-2-[(2-{3-(trifluoromethyl)pyridin-2-yl}amino)ethyl]-amino)ethyl]amino)sulfonyl]thien-2-yl}methyl)benzamide

N-({5-[(2-[4-(1H-1,2,3-benzotriazol-1-yl)piperidin-1-yl]-2-oxoethyl)amino)sulfonyl]thien-2-yl}methyl)-4-chlorobenzamide

12. (Amended) Use according to claim 10 for the treatment or prevention of disorders associated with abnormal expression or activity of JNK2 and/or 3.

13. (Amended) Use of a sulfonyl amino acid derivative according to formula I in particular claim 10 for the treatment of neuronal disorders including epilepsy; Alzheimer's disease, Huntington's disease, Parkinson's disease; retinal diseases, spinal cord injury, head trauma.

14. (Amended) Use of a sulfonyl amino acid derivative according to formula I in particular according to claim 10 for the treatment of autoimmune diseases including Multiple Sclerosis, inflammatory bowel disease (IBD), rheumatoid arthritis, asthma, septic shock, transplant rejection.

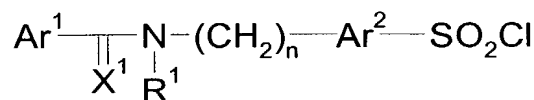
15. (Amended) Use of a sulfonyl amino acid derivative according to formula I in particular according to claim 10 for the treatment of cancer including breast-, colorectal-, pancreatic cancer.

16. (Amended) Use of a sulfonyl amino acid derivative according to formula I in particular according to claim 10 for the treatment of cardiovascular diseases including stroke, arterosclerosis, myocordial infarction, myocordial reperfusion injury.

17. (Amended) A pharmaceutical composition containing at least one sulfonyl amino acid derivative according to claim 1 and a pharmaceutically acceptable carrier, diluent or excipient thereof.

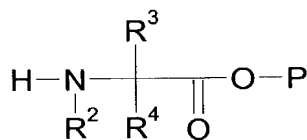
18. (Amended) Process for the preparation of a sulfonyl amino acid derivative according to claim 1 comprising or consisting of the steps of:

a) preparing a sulfonyl compound V,



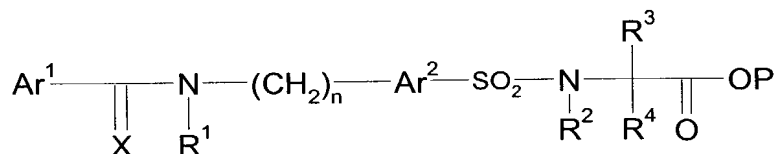
V

b) reacting it with the protected amino acid compound VIII



VIII

thus leading to a compound



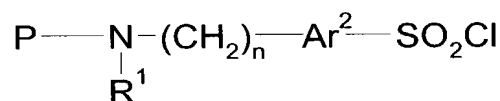
IX

c) said compound IX is subjected to a deprotection and finally

d) a coupling.

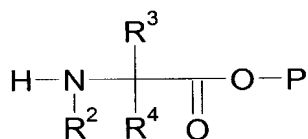
19. (Amended) Process for the preparation of the sulfonyl amino acid derivatives according to claim 1 comprising or consisting of the steps of:

a) preparing a protected sulfonyl compound VII



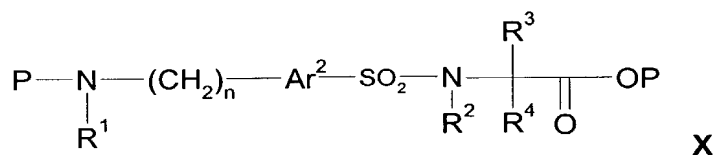
VII

b) reacting it with the protected amino acid compound VIII



VIII

thus leading to a compound



- e) followed by deprotection;
- f) coupling;
- g) deprotection, and
- h) acylation.

Please add the following new claims.

20. (New) A sulfonyl amino acid derivative according to claim 2, wherein n is 1.

21. (New) A sulfonyl amino acid derivative according to claim 2, wherein Ar¹ and Ar² are independently selected from the group comprising or consisting of phenyl, thienyl, furyl, pyridyl, said residues being optionally substituted by at least one substituted or unsubstituted C₁-C₆-alkyl, like trihalomethyl, substituted or unsubstituted C₁-C₆-alkoxy, substituted or unsubstituted C₂-C₆-alkenyl, substituted or unsubstituted C₂-C₆-alkynyl, amino, acylamino, aminocarbonyl, substituted or unsubstituted C₁-C₆-alkoxycarbonyl, aryl, carboxyl, cyano, halogen, hydroxy, nitro, acyloxy, acylamino, sulfoxy, sulfonyl, substituted or unsubstituted C₁-C₆- thioalkoxy.

22. (New) A sulfonyl amino acid derivative according to claim 2, wherein at least one of R³ and/or R⁴ is selected from the group consisting of the following natural amino acid residues : alanyl, arginyl, asparaginy, aspartyl, cysteinyl, glu-taminyl, glutamyl, glycyl, histidyl, isoleucyl, leucyl, lysyl, methionyl, phenylalanyl, prolyl, seryl, threonyl, tryptophanyl, tyrosyl, valyl.

23. (New) A sulfonyl amino acid derivative according to claim 2, wherein

Ar¹ is an unsubstituted or substituted phenyl, preferably 4-chlorophenyl, X is O, R¹, R², R³ and R⁴ are hydrogen, n is 1, Ar² is thienyl, R⁵ is H or C₁-C₆-alkyl;

R⁶ is selected from the group comprising or consisting of H, a substituted or unsubstituted C₁-C₆-aliphatic alkyl - e.g. a C₁-C₆-alkylamino aryl, a C₁-C₆-alkylamino

heteroaryl, a substituted or unsubstituted cyclic C₄-C₈-alkyl containing optionally 1-3 heteroatoms and being optionally fused with an unsubstituted or substituted aryl or heteroaryl; or R⁶ is an unsubstituted or substituted aryl or heteroaryl;

said aryl or heteroaryl groups are optionally substituted by substituted or unsubstituted C₁-C₆-alkyl, like trihalomethyl, substituted or unsubstituted C₁-C₆-alkoxy, substituted or unsubstituted C₂-C₆-alkenyl, substituted or unsubstituted C₂-C₆-alkynyl, amino, acylamino, aminocarbonyl, substituted or unsubstituted C₁-C₆-alkoxycarbonyl, aryl, carboxyl, cyano, halogen, hydroxy, nitro, sulfoxy, C₁-C₆-thioalkoxy; or

R⁵ and R⁶ taken together could form an unsubstituted or substituted 4-8-membered saturated cyclic alkyl or heteroalkyl group, e.g. an unsubstituted or substituted piperidino group.

24. (New) A sulfonyl amino acid derivative according to claim 2, wherein

R⁵ is H; and R⁶ is a C₁-C₆-alkyl which is substituted by an aryl, an heteroaryl group or an aminoaryl, aminoheteroaryl, aryloxy, heteroaryloxy, whereby said aryl and heteroaryl groups are optionally substituted by substituted or unsubstituted C₁-C₆-alkyl, like trihalomethyl, substituted or unsubstituted C₁-C₆-alkoxy, substituted or unsubstituted C₂-C₆-alkenyl, substituted or unsubstituted C₂-C₆-alkynyl, amino, acylamino, aminocarbonyl, substituted or unsubstituted C₁-C₆-alkoxycarbonyl, substituted or unsubstituted aryl, carboxyl, cyano, halogen, hydroxy, nitro, sulfoxy, C₁-C₆-thioalkoxy.

25. (New) A sulfonyl amino acid derivative according to claim 24 which is selected from the following group :

4-chloro-N-({5-[(2-({3-chloro-5-(trifluoromethyl)pyridin-2-yl}amino)ethyl)-amino]-2-oxoethyl}amino)sulfonyl]thien-2-yl)methyl)benzamide

4-chloro-N-[(5-[(2-({5-nitropyridin-2-yl}amino)ethyl)amino]-2-oxoethyl)-amino]sulfonyl]thien-2-yl)methyl]benzamide

[illegible]

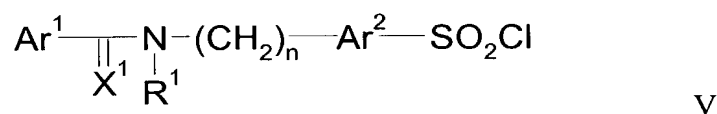
N-({5-[(2-[4-(1H-1,2,3-benzotriazol-1-yl)piperidin-1-yl]-2-oxoethyl)amino]-sulfonyl}thien-2-yl)methyl)-4-chlorobenzamide

4-chloro-N-[(5-[[[(2-oxo-2-{3-[(trifluoromethyl)sulfonyl]anilino}ethyl)amino]-sulfonyl]thien-2-yl)methyl]benzamide.

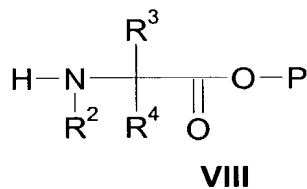
26. (New) A pharmaceutical composition containing at least one sulfonyl amino acid derivative according to claim 2 and a pharmaceutically acceptable carrier, diluent or excipient thereof.

27. (New) Process for the preparation of a sulfonyl amino acid derivative according to claim 2 comprising or consisting of the steps of:

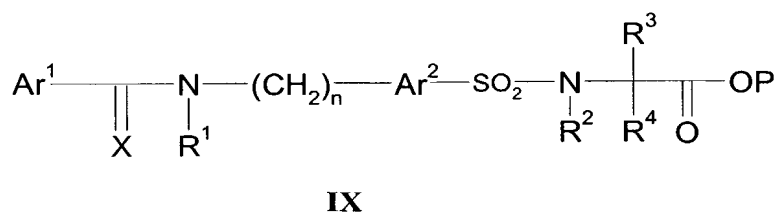
a) preparing a sulfonyl compound V,



b) reacting it with the protected amino acid compound VIII



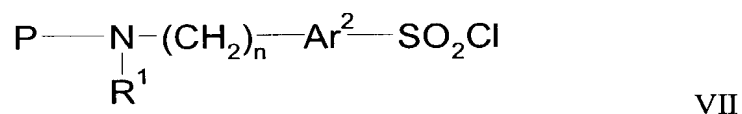
thus leading to a compound



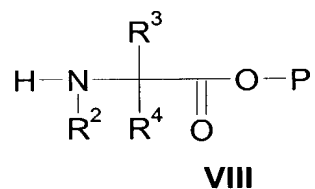
- c) said compound IX is subjected to a deprotection and finally
- d) a coupling.

28. (New) Process for the preparation of the sulfonyl amino acid derivatives according to claim 2 comprising or consisting of the steps of:

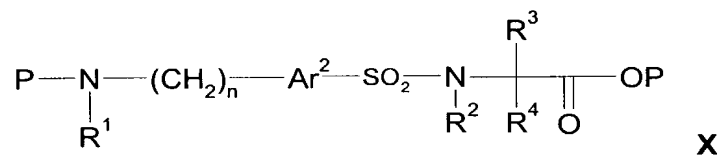
- a) preparing a protected sulfonyl compound VII



- b) reacting it with the protected amino acid compound VIII



thus leading to a compound



- e) followed by deprotection;
- f) coupling;
- g) deprotection, and
- h) acylation.

[illegible]


22850
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220316US-236532-236533-0-PCT

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MAIER & NEUSTADT, P.C.

Norman F. Oblon
Attorney of Record
Registration No. 24,618



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NFO:SUK\1a

220316US-236532-236533-0-PCT

Marked-Up Copy

Serial No: _____

Amendment Filed on: 3-21-2002

IN THE CLAIMS

Please amend the claims as follows.

--3. (Amended) A sulfonyl amino acid derivatives according to claim 1 [or 2],
wherein n is 1.

4. (Amended) A sulfonyl amino acid derivative according to [any of the preceding claims] claim 1, wherein Ar¹ and Ar² are independently selected from the group comprising or consisting of phenyl, thienyl, furyl, pyridyl, said residues being optionally substituted by at least one substituted or unsubstituted C₁-C₆-alkyl, like trihalomethyl, substituted or unsubstituted C₁-C₆-alkoxy, substituted or unsubstituted C₂-C₆-alkenyl, substituted or unsubstituted C₂-C₆-alkynyl, amino, acylamino, aminocarbonyl, substituted or unsubstituted C₁-C₆-alkoxycarbonyl, aryl, carboxyl, cyano, halogen, hydroxy, nitro, acyloxy, acylamino, sulfoxy, sulfonyl, substituted or unsubstituted C₁-C₆- thioalkoxy.

5. (Amended) A sulfonyl amino acid derivative according to [any of the preceding claims] claim 1, wherein at least one of R³ and/or R⁴ is selected from the group consisting of the following natural amino acid residues : alanyl, arginyl, asparaginy, aspartyl, cysteinyl, glu-taminyl, glutamyl, glycyl, histidyl, isoleucyl, leucyl, lysyl, methionyl, phenylalanyl, prolyl, seryl, threonyl, tryptophanyl, tyrosyl, valyl.

6. (Amended) A sulfonyl amino acid derivative according to [any of the preceding claims] claim 1, wherein

Ar¹ is an unsubstituted or substituted phenyl, preferably 4-chlorophenyl, X is O, R¹, R², R³ and R⁴ are hydrogen, n is 1, Ar² is thienyl, R⁵ is H or C₁-C₆-alkyl;

R⁶ is selected from the group comprising or consisting of H, a substituted or unsubstituted C₁-C₆-aliphatic alkyl - e.g. a C₁-C₆-alkylamino aryl, a C₁-C₆-alkylamino heteroaryl, a substituted or unsubstituted cyclic C₄-C₈-alkyl containing optionally 1-3 heteroatoms and being optionally fused with an unsubstituted or substituted aryl or heteroaryl; or R⁶ is an unsubstituted or substituted aryl or heteroaryl;

said aryl or heteroaryl groups are optionally substituted by substituted or unsubstituted C₁-C₆-alkyl, like trihalomethyl, substituted or unsubstituted C₁-C₆-alkoxy, substituted or unsubstituted C₂-C₆-alkenyl, substituted or unsubstituted C₂-C₆-alkynyl, amino, acylamino, aminocarbonyl, substituted or unsubstituted C₁-C₆-alkoxycarbonyl, aryl, carboxyl, cyano, halogen, hydroxy, nitro, sulfoxy, C₁-C₆-thioalkoxy; or

R⁵ and R⁶ taken together could form an unsubstituted or substituted 4-8-membered saturated cyclic alkyl or heteroalkyl group, e.g. an unsubstituted or substituted piperidino group.

7. (Amended) A sulfonyl amino acid derivative according to [any of the preceding claims] claim 1, wherein

R⁵ is H; and R⁶ is a C₁-C₆-alkyl which is substituted by an aryl, an heteroaryl group or an aminoaryl, aminoheteroaryl, aryloxy, heteroaryloxy, whereby said aryl and heteroaryl groups are optionally substituted by substituted or unsubstituted C₁-C₆-alkyl, like trihalomethyl, substituted or unsubstituted C₁-C₆-alkoxy, substituted or unsubstituted C₂-C₆-alkenyl, substituted or unsubstituted C₂-C₆-alkynyl, amino, acylamino, aminocarbonyl, substituted or unsubstituted C₁-C₆-alkoxycarbonyl, substituted or unsubstituted aryl, carboxyl, cyano, halogen, hydroxy, nitro, sulfoxy, C₁-C₆-thioalkoxy.

9. (Amended) A sulfonyl amino acid derivative according to [any of the preceding claims] claim 1 which is selected from the following group :

4-chloro-N-({5-[(2-[(2-[(3-chloro-5-(trifluoromethyl)pyridin-2-yl]amino)ethyl)-amino]-2-oxoethyl]amino)sulfonyl]thien-2-yl}methyl)benzamide

4-chloro-N-[(5-[(2-[(2-[(5-nitropyridin-2-yl]amino)ethyl]amino)-2-oxoethyl)-amino]sulfonyl]thien-2-yl)methyl]benzamide

4-chloro-N-({5-[(2-oxo-2-[(2-[(3-(trifluoromethyl)pyridin-2-yl]amino)ethyl)-amino]ethyl}amino)sulfonyl]thien-2-yl}methyl)benzamide

4-chloro-N-({5-[(2-oxo-2-[(2-[(5-(trifluoromethyl)pyridin-2-yl]amino)ethyl)-amino]ethyl}amino)sulfonyl]thien-2-yl}methyl)benzamide

N-({5-[(2-[4-(1H-1,2,3-benzotriazol-1-yl)piperidin-1-yl]-2-oxoethyl}amino)-sulfonyl]thien-2-yl}methyl)-4-chlorobenzamide

4-chloro-N-[(5-[(2-oxo-2-{3-[(trifluoromethyl)sulfonyl]anilino}ethyl)amino]-sulfonyl]thien-2-yl)methyl]benzamide.

12. (Amended) Use according to claim 10 [or 11] for the treatment or prevention of disorders associated with abnormal expression or activity of JNK2 and/or 3.

13. (Amended) Use of a sulfonyl amino acid derivative according to formula I in particular [according to any of claims 10 to 12] claim 10 for the treatment of neuronal disorders including epilepsy; Alzheimer's disease, Huntington's disease, Parkinson's disease; retinal diseases, spinal cord injury, head trauma.

14. (Amended) Use of a sulfonyl amino acid derivative according to formula I in particular according to [any of claims 10 to 12] claim 10 for the treatment of autoimmune diseases including Multiple Sclerosis, inflammatory bowel disease (IBD), rheumatoid arthritis, asthma, septic shock, transplant rejection.

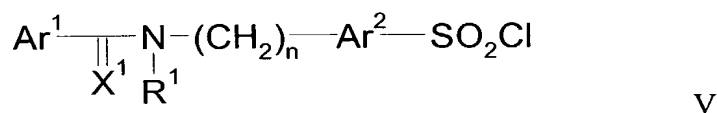
15. (Amended) Use of a sulfonyl amino acid derivative according to formula I in particular according to [any of claims 10 to 12] claim 10 for the treatment of cancer including breast-, colorectal-, pancreatic cancer.

16. (Amended) Use of a sulfonyl amino acid derivative according to formula I in particular according to [any of claims 10 to 12] claim 10 for the treatment of cardiovascular diseases including stroke, arterosclerosis, myocordial infarction, myocordial reperfusion injury.

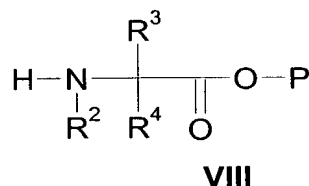
17. (Amended) A pharmaceutical composition containing at least one sulfonyl amino acid derivative according to [any of the claims 1 to 9] claim 1 and a pharmaceutically acceptable carrier, diluent or excipient thereof.

18. (Amended) Process for the preparation of a sulfonyl amino acid derivative according to [any of the claims 1 to 9] claim 1 comprising or consisting of the steps of:

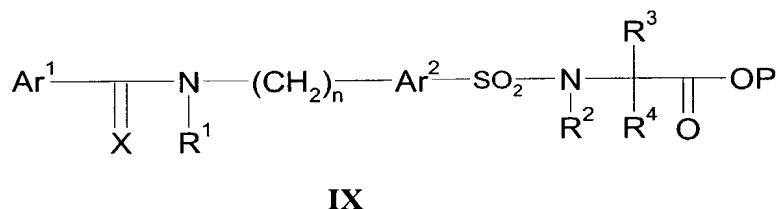
e) preparing a sulfonyl compound V,



f) reacting it with the protected amino acid compound VIII



thus leading to a compound

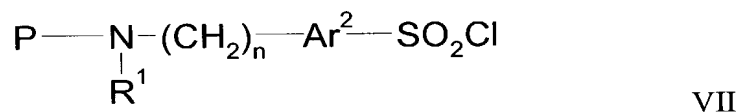


g) said compound IX is subjected to a deprotection and finally

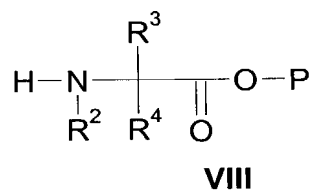
h) a coupling.

19. (Amended) Process for the preparation of the sulfonyl amino acid derivatives according to [any of the claims 1 to 9] claim 1 comprising or consisting of the steps of:

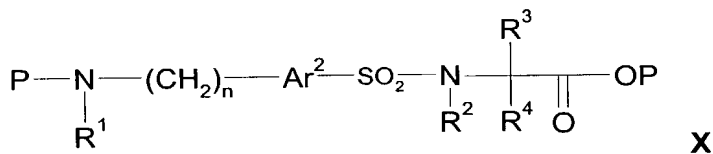
a) preparing a protected sulfonyl compound VII



b) reacting it with the protected amino acid compound VIII



thus leading to a compound



e) followed by deprotection;

f) coupling;

g) deprotection, and

h) acylation.--

Claims 20-28 (New).

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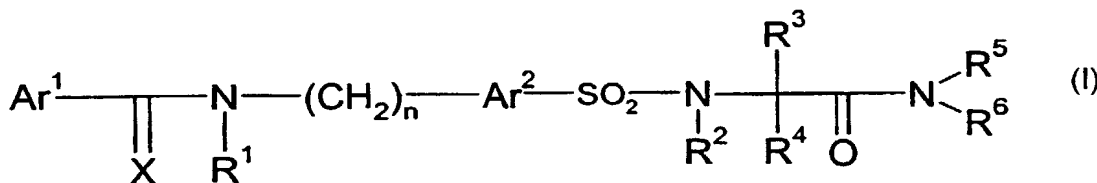
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(54) Title: PHARMACEUTICALLY ACTIVE SULFONYL AMINO ACID DERIVATIVES



(57) Abstract: The present invention is related to sulfonyl amino acid derivatives of formula (I), notably for use as pharmaceutically active compounds, as well as to pharmaceutical formulations containing such sulfonyl amino acid derivatives. Said sulfonyl amino acid are efficient modulators of the JNK pathway, they are in particular efficient inhibitors of JNK 2 and 33. The present invention is furthermore related to novel sulfonyl amino acid derivatives as well as to methods of their preparation.

WO 01/23379 A1

Declaration, Power of Attorney and Petition

Page 1 of 4

WE (I) the undersigned inventor(s), hereby declare(s) that:

My residence, post office address and citizenship are as stated below next to my name,

We (I) believe that we are (I am) the original, first and joint (sole) inventor(s) of the subject matter which is claimed and for which a patent is sought on the invention entitled

PHARMACEUTICALLY ACTIVE SULFONYL AMINO ACID DERIVATIVES

the specification of which

☐ is attached hereto.

☒ was filed on 21 March 2002 as

Application Serial No. 10/088,090

and amended on _____

☒ was filed as PCT international application

Number PCT/IB00/01382

on 28 September 2000,

and was amended under PCT Article 19

on _____ (if applicable).

We (I) hereby state that we (I) have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

We (I) acknowledge the duty to disclose information known to be material to the patentability of this application as defined in Section 1.56 of Title 37 Code of Federal Regulations.

We (I) hereby claim foreign priority benefits under 35 U.S.C. § 119(a)-(d) or § 365(b) of any foreign application(s) for patent or inventor's certificate, or § 365(a) of any PCT International application which designated at least one country other than the United States, listed below and have also identified below, by checking the box, any foreign application for patent or inventor's certificate, or PCT International application having a filing date before that of the application on which priority is claimed. Prior Foreign Application(s)

| Application No. | Country | Day/Month/Year | Priority Claimed |
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| <u>99810871.6</u> | <u>Europe</u> | <u>28 September 1999</u> | <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No |
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| _____ | _____ | _____ | <input type="checkbox"/> Yes <input type="checkbox"/> No |
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(Application Number)

(Filing Date)

(Application Number)

(Filing Date)

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| _____ | _____ | _____ |
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as our (my) attorneys, with full powers of substitution and revocation, to prosecute this application and to transact all business in the Patent Office connected therewith; and we (I) hereby request that all correspondence regarding this application be sent to



We (I) declare that all statements made herein of our (my) own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

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10/088090
27 JUN 2002

220316US0PCT

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Page 1 of 4

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10/01

Serge HALAZY
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Mailing Address: Same as above

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✓ [Signature]
Signature of Inventor

✓ May 24th 2002
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220316US0PCT

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Date

Signature of Inventor

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